Please include the amended SEQUENCE LISTING.

REMARKS

The foregoing amendments and these remarks are in response to the Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The specification and SEQUENCE LISTING have been amended in the patent application and an amended SEQUENCE LISTING has been provided. The affected sections of the specification are shown on a separate copy entitled Marked-Up Version to show the changes made. Applicants provide a computer readable form (CRF) copy of the amended SEQUENCE LISTING, an initial paper or compact disc copy of the SEQUENCE LISTING, as well as this Amendment directing its entry into the application. Applicants also provide a Statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CRF 1.821(f).

Applicants submit that no new matter is entered by this Preliminary Amendment and respectfully request entry of the amendment and examination on the merits. A separate clean copy of the SEQUENCE LISTING is attached. A separate clean set of the substitute pages is attached.

Respectfully submitted,

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vector, bacteria were transformed using electroporation, and more than 100 clones were obtained for further analysis. 96 of these clones were selected for detailed analysis with insert amplification using PCR for each of the 96 selected clones, and finally, 96-dot cDNA arrays were prepared for further screening.

In order to avoid false positives, a 96-dot cDNA array was hybridized with both forward- and reverse-subtracted probes. Six clones were selected for further detailed analysis. Northern blot analysis is not necessarily performed, since it requires microgram amounts of stem/progenitor cell-specific mRNA. DNA sequence analysis of the fragments was performed, and searches were also made for homology of selected fragments to previously known sequences reported in databases (EMBL, GenBank PDP and SWISS-PROT) using the BlastN/X software package (Table 5).

Table 5

Summary of Suppression Subtractive Hybridization (SSH) Fragments

Clone Name	Insert Length (bp)	BLAST Homology	% of Homology Identities	Positives	Accession Number
A4	412	Human cytochrome oxidase subunit 1	100		AF035429
A11	439	Human calcyclin-binding protein	100		AF057356
C6	204	No significant	N/A		N/A
C9	258	No significant	N/A		N/A
C10	260	3'untranslated region of human stromelysin	98		U78045
E11	270	Myc-type, 'helix-loop-helix'dimerization domain signature	N/A		N/A
F4	268	1) Human focal adhesion kinase 2	34	46	Q14289
		2) Homeotic protein spalt-major	33	42	P39770
		3) Mouse hypothetical protein ORF-1137	32	41	P11260

Clone Name	Insert Length (bp)	BLAST Homology	% of Homology	Accession Number
F9	480	Human intercellular adhesion molecule-3 precursor	35 48	P32942

5.8.1 CLONE DESCRIPTION

Clone A4 was shown to be identical to human cytochrome oxidase subunit 1, which is essential for energy conversion in all aerobic organisms.

Clone A11 was shown to be identical to human calcyclin-binding protein (CacyBP), which was identified in human and mouse brains and Ehrlich ascites tumor (EAT) cells and is expressed predominantly there. Because CacyBP, like calcyclin, is present in the brain, the interaction of these two proteins might be involved in calcium signaling pathways in neurol tissue.

Clone C6 had no significant homology to previously sequences reported in databases.

Clone C9 had no significant homology to previously sequences reported in databases.

Clone C10 had strong homology to 3' untranslated region of stromelysin, human metalloproteinase (MMP) responsible for the breakdown of proteins of connective tissue. Through this action they play an important role in growth, development and tissue repair. Recent studies also suggest that MMPs are utilized in cancer, facilitating both local tumor invasion and metastasis.

Clone E11 did not have any strong homology, but exhibits a Myc-type, 'helix-loop-helix'dimerization domain signature. The myc genes are thought to play a role in cellular differentiation and proliferation.

Clone F4 revealed homologies to:

1) Human focal adhesion kinase 2 (FADK 2) (Proline-rich tyrosine kinase 2) (Cell adhesion kinase Beta) (CAK Beta)

```
Query: 201
KDLPPEQERKRRERTPKNLGNRDEHRTERKRRTPIPQPTHWGPEHSRPRWNMGPPLKTLL 22
KD+  EQER R RTPK L              T   +P    P+ SRP++   PP +T L
KDIAMEQERNARYRTPKIL----------EPTAFQEPP--PKPSRPKYR--PPPQTNL
Sbjct 730:

687 Query: 21 M
           +
Sbjct: 731 L
```

This protein is involved in calcium induced ion channel regulation, and activation of the MAP kinase signaling pathway. It may represent an important signaling intermediary between neuropeptide-activated receptors or neurotransmitters that increase calcium flux, as well as downstream signals that regulate neuronal activity.

2) Salm drome homeotic protein spalt-major

```
Query: 195 LPPEQERKRRERTPKNLGNRDEHRTERKRRTPIPQPTHWGPEHSRPRWNMGPPL
34      (SEQ ID NO: 5)
LP E   K       +     +++HR E  RRTP P       H  P H R       PP+
Sbjct: 634                    (SEQ ID NO: 6)
LPLEVRIKEERVEEQEQVKQEDHRIE-PRRTPSPSSEHRSPHHHRHSHMGYPPV 686
(SEQ ID NO: 7)
```

This is a transcriptional factor encoded by the spalt major (salm) gene, which is expressed during Drosophila embryogenesis. This protein is found in a broad wedge centered over the decapentaplegic (dpp) stripe, and is one target of Dpp signaling.

3) Mouse hypothetical protein ORF-1137

```
Query: 183 QERKRRERTPKNLGNRDEHRTERKRRTPIPQPTHWGPEHSRPRWNMGPPLKTLLM
19      (SEQ ID NO: 8)
Q  K + + P N      +H     +R TP P       P H      N+ P LKT LM
Sbjct: 22
QMAKGKRKNPTN---RNQDHSPSSERSTPTPP-----SPGHPNTTENLDPDLKTFLM 70
 (SEQ ID NO: 9)
```

Clone F9 was found to be homologous to human intercellular adhesion molecule-3 precursor

```
Query: 44
(SEQ ID NO: 10) EAPTPCLAVSAKTTVGLTEVSLCSCAPSQPLLNGLRV=-----GSQFFCGACLEVSGYYLK
208
E  T  ++  A   V +T   + + AP QP    L       G  FFC A LE V G +L
Sbjct: 328 EGSTVTVSCMAGARVQVTLDGVPAAAPGQPAQLQLNATESDDGRSFFCSATLEVDGEFLH
387   (SEQ ID NO: 11)

Query: 209 DFSLIRLPFL 238   (SEQ ID NO. 12)
            S ++L  L      (SEQ ID NO. 13)
Sbjct: 388 RNSSVQLRVL 397
```

Human intercellular adhesion molecule-3 (ICAM)-3 or CDw50 differentiation antigen is expressed by hematopoietic cells, and not by other cells examined to date. Immunochemical, functional, and protein sequencing studies have shown that this protein presumably plays an important role in the immune response.

This method may be used to perform differential screening of neurospheres at different stages of development/ differentiation, and such differential screening can disclose potential

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Query: 201

KDLPPEQERKRRERTPKNLGNRDEHRTERKRRTPIPQPTHWGPEHSRPRWNMGPPLKTLL
(SEQ ID NO:1)
KD+ EQER R RTPK L T +P P+ SRP++ PP +T L
(SEQ ID NO:2) (SEQ ID NO:3)
KDIAMEQERNARYRTPKIL——————EPTAFQEPP——PKPSRPKYR—PPPQTNL
(SEQ ID NO:4)

Sbjct 730:

687 Query: 21 M
+
Sbjct: 731 L

This protein is involved in calcium induced ion channel regulation, and activation of the MAP kinase signaling pathway. It may represent an important signaling intermediary between neuropeptide-activated receptors or neurotransmitters that increase calcium flux, as well as downstream signals that regulate neuronal activity.

2) Salm drome homeotic protein spalt-major

Query: 195 LPPEQERKRRERTPKNLGNRDEHRTERKRRTPIPQPTHWGPEHSRPRWNMGPPL
34 (SEQ ID NO: 5)
LP E K + +++HR E RRTP P H P H R PP+
(SEQ ID NO. 6)
Sbjct:634
LPLEVRIKEERVEEQEQVKQEDHRIE-PRRTPSPSSEHRSPHHHRHSHMGYPPV 686
(SEQ ID NO. 7)

c1
Cont

This is a transcriptional factor encoded by the spalt major (salm) gene, which is expressed during Drosophila embryogenesis. This protein is found in a broad wedge centered over the decapentaplegic (dpp) stripe, and is one target of Dpp signaling.

3) Mouse hypothetical protein ORF-1137

Query: 183 QERKRRERTPKNLGNRDEHRTERKRRTPIPQPTHWGPEHSRPRWNMGPPLKTLLM
(SEQ ID NO. 8)
19
Q K + + P N +H +R TP P P H N+ P LKT LM
Sbjct: 22
QMAKGKRKNPTN—RNQDHSPSSERSTPTPP———SPGHPNTTENLDPDLKTFLM 70
(SEQ ID NO. 9)

Clone F9 was found to be homologous to human intercellular adhesion molecule-3 precursor

```
Query:  44
EAPTPCLAVSAKTTVGLTEVSLCSCAPSQPLLNGLRV———GSQFFCGACLEVSGYYLK
(SEQ ID NO. 10)
208
E  T  ++  A   V +T   + + AP QP    L      G  FFC A LE V G +L
Sbjct: 328 EGSTVTVSCMAGARVQVTLDGVPAAAPGQPAQLQLNATESDDGRSFFCSATLEVDGEFLH
      (SEQ ID NO.11)
387

Query:  209 DFSLIRLPFL (SEQ ID NO. 12) 238
              S ++L  L
Sbjct:  388 RNSSVQLRVL (SEQ ID NO.13)  397
```

C1 Cont

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